## WO 2004/106941 PCT/EP2004/005786 CLAIMS

- 1. A method of screening for and /or diagnosis of a cardiovascular disorder in a subject, comprising the steps of:
  - a) detecting and /or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
    - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NO: 1-2, 5-6, 13, and 20-21;
    - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs: 1-2, 5-6, 13, and 20-21; and
    - iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and
  - b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control is indicative of a cardiovascular disorder.
- 2. A method of predicting a cardiovascular disorder in a subject, comprising the steps of:
  - a) detecting and /or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from:
    - a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NO: 1-2, 5-6, 13, and 20-21;
    - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs: 1-2, 5-6, 13, and 20-21; and
    - iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and
  - b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control indicates a risk of developing a cardiovascular disorder.
- 3. The method of claim 1 or 2, wherein the level of two or more of the polypeptides of claim 1 or 2 are detected and /or quantified in a biological sample from said subject.
- 4. The method of any one of claims 1 to 3, wherein said cardiovascular disorder is Coronary Artery Disease (CAD).

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- 5. The method of any one of claims 1 to 4, wherein said biological sample is plasma.
- 6. The method of any one of claims 1 to 5, wherein said polypeptide is detected and /or quantified by mass spectrometry.
- 7. The method of any one of claims 1 to 5, wherein said polypeptide is detected and /or quantified by Enzyme-Linked Immuno Sorbent Assay.
- 8. An isolated polypeptide comprising the amino acid sequence selected from selected from one of the groups consisting of SEQ ID NOs: 1-4, 5-12, 13-19 and 20-25, wherein said polypeptide is fused to a heterologous polypeptide sequence.
- An anti-Cardiovascular disorder Plasma Polypeptide (CPP) antibody that selectively binds to a
  polypeptide comprising the amino acid sequence selected from selected from one of the groups
  consisting of SEQ ID NOs: 1-4, 5-12, 13-19 and 20-25.
- 10. A method of binding an antibody to a Cardiovascular disorder Plasma Polypeptide (CPP) comprising the steps of:
  - i) contacting the antibody of claim 9 with a biological sample under conditions that permit antibody binding; and
  - ii) removing contaminants.
- 11. The method of claim 10, wherein said antibody is attached to a label group.
- 12. The method of claim 10, wherein said sample is human plasma.
- 13. A method of identifying a Cardiovascular disorder Plasma Polypeptide (CPP) modulator comprising the steps of:
  - i) contacting a test compound with a CPP comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NOs: 1-4, 5-12, 13-19 and 20-25 under sample conditions permissive for at least one CPP biological activity;
  - ii) determining the level of said at least one CPP biological activity;
  - iii) comparing said level to that of a control sample lacking said test compound; and
  - iv) selecting a test compound which causes said level to change for further testing as a CPP modulator for the prophylactic and/or therapeutic treatment of cardiovascular disorders.

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14. A method of identifying a modulator of a cardiovascular disorder comprising the steps of:

- (a) administering a candidate agent to a non-human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder;
- (b) administering the candidate agent of (a) to a matched control non-human animal not predisposed to be affected or not being affected by the cardiovascular disorder;
- (c) detecting and /or quantifying the level of a polypeptide in a biological sample obtained from the non-human test animal of step (a) and from the control animal of step (b), wherein the polypeptide is selected from:
  - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NO: 1-2, 5-6, 13, and 20-21;
  - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs: 1-2, 5-6, 13, and 20-21; and
  - iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and
- (d) comparing the levels of the polypeptide of step (c); wherein a displacement of the level of the polypeptide in the biological sample obtained from the non-human test animal towards the level of the polypeptide in the biological sample obtained from the control animal indicates that the candidate agent is a modulator of the cardiovascular disorder.
- 15. The method of claim 14, wherein the non-human test animal which is predisposed to be affected or which is affected by the cardiovascular disorder comprises an increased plasma level of a polypeptide selected from:
  - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NO: 1-2, 5-6, 13, and 20-21;
  - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs: 1-2, 5-6, 13, and 20-21; and
  - iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long.

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16. A method for monitoring the efficacy of a treatment of a subject having or at risk of developing a cardiovascular disorder with an agent, the method comprising:

- (a) obtaining a pre-administration biological sample from the subject prior to administration of the agent;
- (b) detecting and /or quantifying the level of a polypeptide in the biological sample from said subject, wherein the polypeptide is selected from:
  - i) a polypeptide comprising the amino acid sequence selected from one of the groups consisting of SEQ ID NO: 1-2, 5-6, 13, and 20-21;
  - ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NOs: 1-2, 5-6, 13, and 20-21; and
  - iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long; and
- (c) obtaining one or more post-administration biological samples from the subject;
- (d) detecting the level of the polypeptide in the post-administration sample or samples;
- (e) comparing the level of the polypeptide in the pre-administration sample with the level of the polypeptide in the post- administration sample; and
- (f) adjusting the administration of the agent accordingly.